

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptamxgl614

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 JUL 20 Powerful new interactive analysis and visualization software,
STN AnaVist, now available
NEWS 4 AUG 11 STN AnaVist workshops to be held in North America
NEWS 5 AUG 30 CA/CAPLUS - Increased access to 19th century research documents
NEWS 6 AUG 30 CASREACT - Enhanced with displayable reaction conditions
NEWS 7 SEP 09 ACD predicted properties enhanced in REGISTRY/ZREGISTRY
NEWS 8 OCT 03 MATHDI removed from STN
NEWS 9 OCT 04 CA/CAPLUS-Canadian Intellectual Property Office (CIPO) added
to core patent offices
NEWS 10 OCT 06 STN AnaVist workshops to be held in North America
NEWS 11 OCT 13 New CAS Information Use Policies Effective October 17, 2005
NEWS 12 OCT 17 STN(R) AnaVist(TM), Version 1.01, allows the export/download
of CAPLUS documents for use in third-party analysis and
visualization tools

NEWS EXPRESS JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

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result in loss of user privileges and other penalties.

* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 17:18:44 ON 25 OCT 2005

| | | |
|----------------------|------------|---------|
| => file reg | | |
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 17:18:53 ON 25 OCT 2005
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STRUCTURE FILE UPDATES: 24 OCT 2005 HIGHEST RN 865981-77-7
DICTIONARY FILE UPDATES: 24 OCT 2005 HIGHEST RN 865981-77-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

```
*****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*
*****
```

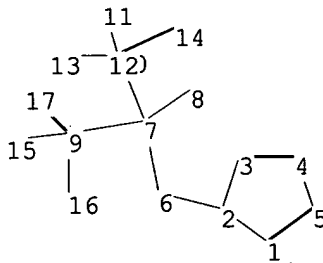
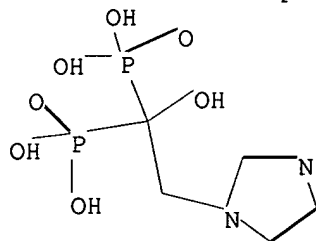
Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Documents and Settings\mgraffeo\My Documents\Critical Data\10531676\compound.str



```
chain nodes :
6 7 8 9 10 11 12 13 14 15 16 17
ring nodes :
1 2 3 4 5
chain bonds :
2-6 6-7 7-8 7-9 7-10 9-15 9-16 9-17 10-11 10-14 12-13
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 2-3 2-6 3-4 4-5 7-8 12-13
exact bonds :
6-7 7-9 7-10
normalized bonds :
9-15 9-16 9-17 10-11 10-14
```

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS

L1 STRUCTURE UPLOADED

=> s l1

SAMPLE SEARCH INITIATED 17:19:12 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 9 TO ITERATE

100.0% PROCESSED 9 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
 BATCH **COMPLETE**
PROJECTED ITERATIONS: 9 TO 360
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l2 full

FULL SEARCH INITIATED 17:19:17 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 189 TO ITERATE

100.0% PROCESSED 189 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L3 0 SEA SSS FUL L1

=> file caplus

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 161.76 | 161.97 |

FILE 'CAPLUS' ENTERED AT 17:20:08 ON 25 OCT 2005
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FILE COVERS 1907 - 25 Oct 2005 VOL 143 ISS 18
FILE LAST UPDATED: 24 Oct 2005 (20051024/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> s l2

L4 0 L2

=> file medline

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 0.45 | 162.42 |

FILE 'MEDLINE' ENTERED AT 17:20:16 ON 25 OCT 2005

FILE LAST UPDATED: 22 OCT 2005 (20051022/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP
RLOAD at an arrow prompt (=>). See also:

<http://www.nlm.nih.gov/mesh/>
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

```
=> s "1-hydroxy-2-(imidazol-1-yl)ethane-1,1-diphosphonic acid"
      3573531 "1"
      61380 "HYDROXY"
      3130230 "2"
      1357 "IMIDAZOL"
      3573531 "1"
      18868 "YL"
      6223 "ETHANE"
      3573531 "1"
      3573531 "1"
      123 "DIPHOSPHONIC"
      1360069 "ACID"
L5      0 "1-HYDROXY-2-(IMIDAZOL-1-YL)ETHANE-1,1-DIPHOSPHONIC ACID"
          ("1" (W) "HYDROXY" (W) "2" (W) "IMIDAZOL" (W) "1" (W) "YL" (W) "ETHANE" (W)
           "1" (W) "1" (W) "DIPHOSPHONIC" (W) "ACID")
```

```
=> file reg
COST IN U.S. DOLLARS                               SINCE FILE      TOTAL
                                                    ENTRY      SESSION
FULL ESTIMATED COST                               0.76      163.18
```

FILE 'REGISTRY' ENTERED AT 17:21:36 ON 25 OCT 2005
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STRUCTURE FILE UPDATES: 24 OCT 2005 HIGHEST RN 865981-77-7
DICTIONARY FILE UPDATES: 24 OCT 2005 HIGHEST RN 865981-77-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

```
*****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005. A new display format, IDERL, is now     *
*
```

* available and contains the CA role and document type information. *
 *

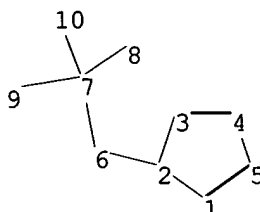
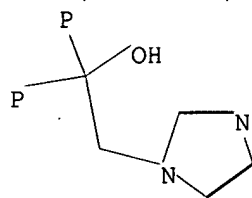
Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Documents and Settings\mgraffeo\My Documents\Critical Data\10531676\compound1.str



chain nodes :
 6 7 8 9 10
 ring nodes :
 1 2 3 4 5
 chain bonds :
 2-6 6-7 7-8 7-9 7-10
 ring bonds :
 1-2 1-5 2-3 3-4 4-5
 exact/norm bonds :
 1-2 1-5 2-3 2-6 3-4 4-5 7-8
 exact bonds :
 6-7 7-9 7-10

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
 10:CLASS

L6 . STRUCTURE UPLOADED

=> s 16

SAMPLE SEARCH INITIATED 17:21:48 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 4 TO ITERATE

100.0% PROCESSED 4 ITERATIONS
 SEARCH TIME: 00.00.01

2 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
 BATCH **COMPLETE**
 PROJECTED ITERATIONS: 4 TO 200
 PROJECTED ANSWERS: 2 TO 124

L7 2 SEA SSS SAM L6

=> s 17 full

FULL SEARCH INITIATED 17:21:54 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 101 TO ITERATE

100.0% PROCESSED 101 ITERATIONS
SEARCH TIME: 00.00.01

47 ANSWERS

L8 47 SEA SSS FUL L6

=> s l8 and rheumatoid
149 RHEUMATOID

L9 0 L8 AND RHEUMATOID

=> s l8 and arthritis
286 ARTHRITIS

L10 0 L8 AND ARTHRITIS

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

171.82

335.00

FILE 'REGISTRY' ENTERED AT 17:23:47 ON 25 OCT 2005
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STRUCTURE FILE UPDATES: 24 OCT 2005 HIGHEST RN 865981-77-7
DICTIONARY FILE UPDATES: 24 OCT 2005 HIGHEST RN 865981-77-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

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conducting SmartSELECT searches.

*
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* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

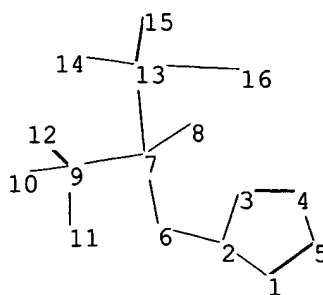
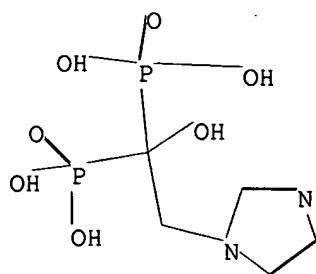
Structure search iteration limits have been increased. See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Documents and Settings\mgraffeo\My Documents\Critical
Data\10531676\compound2.str



```

chain nodes :
6 7 8 9 10 11 12 13 14 15 16
ring nodes :
1 2 3 4 5
chain bonds :
2-6 6-7 7-8 7-9 7-13 9-10 9-11 9-12 13-14 13-15 13-16
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 2-3 2-6 3-4 4-5 7-8
exact bonds :
6-7 7-9 7-13
normalized bonds :
9-10 9-11 9-12 13-14 13-15 13-16

```

```

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS

```

L11 STRUCTURE UPLOADED

```

=> s l11
SAMPLE SEARCH INITIATED 17:23:59 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 9 TO ITERATE

```

```

100.0% PROCESSED          9 ITERATIONS          2 ANSWERS
SEARCH TIME: 00.00.01

```

```

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:   9 TO      360
PROJECTED ANSWERS:      2 TO      124

```

L12 2 SEA SSS SAM L11

```

=> s l12 full
FULL SEARCH INITIATED 17:24:04 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 189 TO ITERATE

```

```

100.0% PROCESSED        189 ITERATIONS          39 ANSWERS
SEARCH TIME: 00.00.01

```

L13 39 SEA SSS FUL L11

```

=> s l13 (L) arthritis
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L13 (L) ARTHRITIS'
286 ARTHRITIS

```

L14 0 L13 (L) ARTHRITIS

=> s l13 and ?immune?

LEFT TRUNCATION IGNORED FOR '?IMMUNE?' FOR FILE 'REGISTRY'
54684 IMMUNE?

L15 0 L13 AND ?IMMUNE?

Left truncation is not valid in the specified search field in the specified file. The term has been searched without left truncation. Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID' would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you used a truncation symbol after a punctuation mark, the system may interpret the truncation symbol as being at the beginning of a term. Implied proximity is used in search fields indexed as single words, for example, the Basic Index.

=> s l13 and ?immune

LEFT TRUNCATION IGNORED FOR '?IMMUNE' FOR FILE 'REGISTRY'
54673 IMMUNE

L16 0 L13 AND ?IMMUNE

Left truncation is not valid in the specified search field in the specified file. The term has been searched without left truncation. Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID' would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you used a truncation symbol after a punctuation mark, the system may interpret the truncation symbol as being at the beginning of a term. Implied proximity is used in search fields indexed as single words, for example, the Basic Index.

=> s l13 and (immune or autoimmune)

54673 IMMUNE
93 AUTOIMMUNE

L17 0 L13 AND (IMMUNE OR AUTOIMMUNE)

=> s l13

SAMPLE SEARCH INITIATED 17:25:59 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 9 TO ITERATE

100.0% PROCESSED 9 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
 BATCH **COMPLETE**
PROJECTED ITERATIONS: 9 TO 360
PROJECTED ANSWERS: 2 TO 124

L18 2 SEA SSS SAM L11

=> s l13 full

FULL SEARCH INITIATED 17:26:15 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 189 TO ITERATE

100.0% PROCESSED 189 ITERATIONS 39 ANSWERS
SEARCH TIME: 00.00.01

L19 39 SEA SSS FUL L11

=> d 30-39 bib abs hitstr

'BIB' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'ABS' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual fields or predefined formats. The predefined substance formats are: (RN = CAS Registry Number)

REG - RN
SAM - Index Name, MF, and structure - no RN
FIDE - All substance data, except sequence data
IDE - FIDE, but only 50 names
SQIDE - IDE, plus sequence data
SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used
SQD - Protein sequence data, includes RN
SQD3 - Same as SQD, but 3-letter amino acid codes are used
SQN - Protein sequence name information, includes RN

CALC - Table of calculated properties
EPROP - Table of experimental properties
PROP - EPROP and CALC

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ABS -- Abstract
APPS -- Application and Priority Information
BIB -- CA Accession Number, plus Bibliographic Data
CAN -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND -- Index Data
IPC -- International Patent Classification
PATS -- PI, SO
STD -- BIB, IPC, and NCL

IABS -- ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB ----- AN, plus Bibliographic Data (original)
OIBIB ----- OBIB, indented with text labels

SBIB ----- BIB, no citations
SIBIB ----- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.

The MAX format is the same as ALL.

The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

HELP DFIELDS -- To see a complete list of individual display fields.
HELP FORMATS -- To see detailed descriptions of the predefined formats.
ENTER DISPLAY FORMAT (IDE):end

=> s 113

SAMPLE SEARCH INITIATED 17:26:38 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 9 TO ITERATE

100.0% PROCESSED 9 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**
PROJECTED ITERATIONS: 9 TO 360
PROJECTED ANSWERS: 2 TO 124

L20 2 SEA SSS SAM L11

=> s 120 full
FULL SEARCH INITIATED 17:26:44 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 189 TO ITERATE

100.0% PROCESSED 189 ITERATIONS 39 ANSWERS
SEARCH TIME: 00.00.01

L21 39 SEA SSS FUL L11

=> file caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 507.85 842.85

FILE 'CAPLUS' ENTERED AT 17:26:47 ON 25 OCT 2005
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FILE COVERS 1907 - 25 Oct 2005 VOL 143 ISS 18
FILE LAST UPDATED: 24 Oct 2005 (20051024/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> s 121
L22 470 L21
=> s 122 and rheumatoid
26974 RHEUMATOID
L23 22 L22 AND RHEUMATOID
=> s 123 and arthritis
38537 ARTHRITIS
L24 22 L23 AND ARTHRITIS

=> d 1-22 bib abs hitstr

L24 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:673327 CAPLUS
DN 143:171327
TI M-CSF-specific monoclonal antibody and derivatives or fragments for drug screening and treatment of osteolytic disease, bone loss, cancer and metastasis
IN Liu, Cheng; Zimmerman, Deborah Lee; Harrowe, Gregory Martin; Koths, Kirston; Kavanaugh, William Michael; Long, Li; Calderon-Cacia, Maria;

Horwitz, Arnold H.
 PA Chiron Corporation, USA; Xoma Technology Ltd.
 SO PCT Int. Appl., 283 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|--|----------|-----------------|----------|
| PI | WO 2005068503 | A2 | 20050728 | WO 2005-US546 | 20050106 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

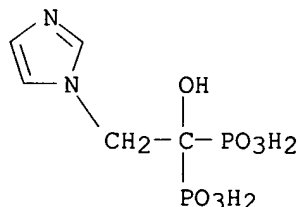
PRAI US 2004-535181P P 20040107
 US 2004-576417P P 20040602

AB M-CSF-specific RX1-based or RX-1 derived antibodies are provided, along with pharmaceutical compns. containing such antibody, kits containing a pharmaceutical composition, and methods of preventing and treating bone loss in a subject afflicted with an osteolytic disease. These antibodies include chimeric antibodies, humanized antibodies, human engineered antibodies, human antibody, antibody conjugates and fragments. Compns. comprising the antibody may also contain a second therapeutic agent, e.g. cancer chemotherapeutic agent such as a bisphosphonate.

IT **118072-93-8**, Zoledronate
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (M-CSF-specific monoclonal antibody and derivs. or fragments for drug screening and treatment of osteolytic disease, bone loss, cancer and metastasis)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



L24 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2005:259887 CAPLUS
 DN 142:336518
 TI Preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivatives as androgen receptor modulators
 IN Meissner, Robert S.; Mitchell, Helen J.
 PA Merck & Co., Inc., USA
 SO PCT Int. Appl., 105 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2005025579 | A1 | 20050324 | WO 2004-US28641 | 20040902 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRAI | US 2003-501664P | P | 20030910 | | |
| OS | MARPAT 142:336518 | | | | |
| GI | | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention discloses preparation of 17 β -heterocyclic-3-oxo-4-aza-5 α -androst-1-ene derivs., such as I [dashed bond = single bond, double bond; X = H, halo; Y, Z = H, alkyl, halo; Y and Z, together with the carbon atom to which they are attached = cyclopropyl; n = 0-3; U, V, W, D = CH, N, provided that at least U, V, W, and D = CH; R1 = H, CF3, carbonyl(alkyl), OH, alkoxy, halo, alkyl, CH2OH, alkylamino; R2 = halo, carbonyl(alkyl), carbonyl(alkenyl), carbonyl(alkynyl), alkenylamino, heterocyclic, etc.], for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 4-azaandrost-1-ene derivative II was reacted with 2,3-diaminopyridine in presence of silver triflate to give 17 β -carboxamide derivative III, which, on heating with polyphosphoric acid, afforded 17 β -imidazopyridinyl-3-oxo-4-aza-5 α -androst-1-ene derivative IV. I are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-wasting, prostate cancer, benign prostatic hyperplasia (BPH), abdominal adiposity, metabolic syndrome, type II diabetes, cancer cachexia, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

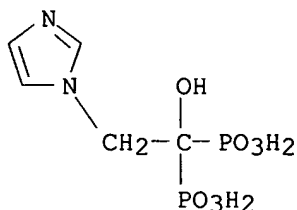
IT 118072-93-8, Zoledronate

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(bone strengthening agents as adjuvant therapeutics; preparation of 17 β -heterocyclic-3-oxo-4-aza-5 α -androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:259881 CAPLUS
DN 142:336517
TI Preparation of 17-heterocyclic-4-aza-5 α -androst-1-en-3-one derivatives for their use as modulators of the androgen receptor in a tissue selective manner
IN Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2005025572 | A1 | 20050324 | WO 2004-US28655 | 20040902 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRAI US 2003-501789P | P | 20030910 | | |
| OS MARPAT 142:336517 | | | | |
| GI | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 17-Heterocyclic-4-aza-5 α -androst-1-en-3-one derivs., such as I [dashed bond = single bond, double bond; X = H, halo; Y, Z = H, alkyl, halo; Y and Z, together with the carbon atom to which they are attached = cyclopropyl; n = 0-3; U, V, W, D = CH, N, S, O; R1 = H, CF3, carbonyl(alkyl), OH, alkoxy, halo, alkyl, CH2OH, alkylamino; R2 = halo, carbonyl(alkyl), carbonyl(alkenyl), carbonyl(alkynyl), alkenylamino, heterocyclic, etc.], were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, II (R = OH) was treated with Et3N, and iso-Bu chloroformate, followed by reaction with N,O-dimethylhydroxylamine hydrochloride to give II [R = N(Me)OMe (III)]. III was converted to 4-aza-5 α -androst-1-en-3,20-dione derivative II (R = Me), and then to bromide II [R = CH2Br (IV)], which was treated with N-butyl-thiourea to afford V. The prepared compds. are useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen

administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-wasting, prostate cancer, benign prostatic hyperplasia (BPH), abdominal adiposity, metabolic syndrome, type II diabetes, cancer cachexia, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

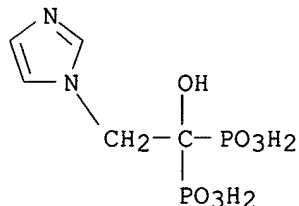
IT 118072-93-8, Zoledronate

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(bone strengthening agents as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5 α -androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:220135 CAPLUS

DN 142:274037

TI Pyrimidine and pyridine derivatives as glycogen synthase kinase 3 (GSK-3) inhibitors for treating or preventing bone loss

IN Bennett, Christina N.; Hankenson, Kurt D.; Harrison, Stephen D.; Longo, Kenneth A.; Macdougald, Ormond A.; Wagman, Allan S.

PA USA

SO U.S. Pat. Appl. Publ., 24 pp.

CODEN: USXXCO

DT Patent

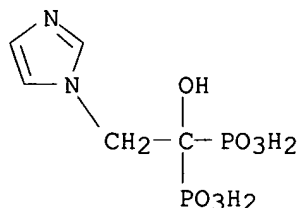
LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|----------|
| PI | US 2005054663 | A1 | 20050310 | US 2004-917707 | 20040813 |
| | WO 2005039485 | A2 | 20050506 | WO 2004-US26355 | 20040813 |
| | WO 2005039485 | A3 | 20050818 | | |
| | W: | | | | |
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| | RW: | | | | |
| | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

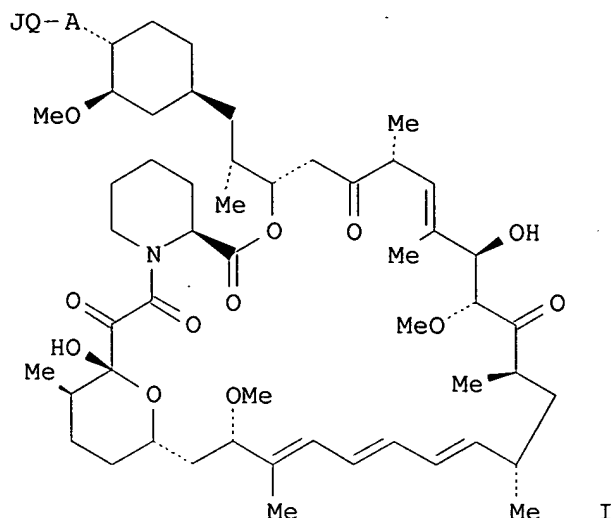
PRAI US 2003-494859P P 20030813

OS MARPAT 142:274037
 AB This invention relates to methods of treating or preventing bone loss by administering to a human or animal subject pyrimidine and pyridine derivs. that inhibit the activity of glycogen synthase kinase 3 (GSK3), to pharmaceutical compns. containing the compds., and to the use of the compds. and compns. alone or in combination with other pharmaceutically active agents. Bone loss is prevented or treated with 6-[[2-[[4-(2,4-dichlorophenyl)-5-(4-methylimidazol-2-yl)pyrimidin-2-yl]amino]ethyl]amino]pyridine-3-carbonitrile (prepared from 2,4-dichlorobenzoyl chloride and 2,4-dimethylimidazole).
 IT 118072-93-8, Zoledronic acid
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (combination therapy with; pyrimidine and pyridine derivs. as glycogen synthase kinase 3 inhibitors for treating or preventing bone loss)
 RN 118072-93-8 CAPLUS
 CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



L24 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2005:122803 CAPLUS
 DN 142:219083
 TI Preparation of phosphorus-containing rapamycin derivatives for use in pharmaceutical compositions as immunosuppressive and anticancer agents
 IN Metcalf, Chester A.; Rozamus, Leonard W.; Wang, Yihan; Bernstein, David L.
 PA USA
 SO U.S. Pat. Appl. Publ., 57 pp., Cont.-in-part of U.S. Ser. No. 635,054.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-------------------|------|----------|-----------------|----------|
| PI | US 2005032825 | A1 | 20050210 | US 2004-862149 | 20040604 |
| | US 2003220297 | A1 | 20031127 | US 2003-357152 | 20030203 |
| | US 2004073024 | A1 | 20040415 | US 2003-635054 | 20030806 |
| PRAI | US 2002-353252P | P | 20020201 | | |
| | US 2002-426928P | P | 20021115 | | |
| | US 2002-428383P | P | 20021122 | | |
| | US 2002-433930P | P | 20021217 | | |
| | US 2003-357152 | A2 | 20030203 | | |
| | US 2003-635054 | A2 | 20030806 | | |
| | | | | | |
| OS | MARPAT 142:219083 | | | | |
| GI | | | | | |



AB Rapamycin derivs. containing phosphorus moiety, such as I [A = O, S, NR₂, absent; Q = V, OV, SV, NR₂, absent; V = aliphatic, heteroaliph., aryl, heteroaryl moiety, such that J is linked to the cyclohexyl ring directly, through A or through VA, OVA, SVA or NR₂VA; J = P(:K)(YR₅)₂, P(YR₅)₂, P(:K)(YR₅)GR₆; K = O, S; Y = O, S, NR₂, bond; R₂, R₅ = aliphatic, heteroaliph., aryl, heteroaryl, H; R₆ = PK(YR₅)YR₅, SO₂YR₅, C(O)YR₅; G = O, S, NR₂, (M)X; M = (un)substituted methylene, alkyl, alkylene; X = 1-6], and pharmaceutically acceptable derivs. thereof, were prepared for therapeutic use as immunosuppressive and anticancer agents. These rapamycin derivs. are useful for treatment of graft vs. host disease, lupus, **rheumatoid arthritis**, diabetes mellitus, myasthenia gravis, multiple sclerosis, psoriasis, dermatitis, eczema, seborrhea, inflammatory bowel disease, pulmonary inflammation, ocular uveitis; adult T-cell leukemia, lymphoma, fungal infections, hyperproliferative restenosis, graft vascular atherosclerosis, coronary artery disease, cerebrovascular disease, arteriosclerosis, atherosclerosis, nonatheromatous arteriosclerosis, or vascular wall damage from cellular events leading toward immune mediated vascular damage, stroke or multi-infarct dementia. Thus, I [A-QJ = OP(O)(OBu)Me] was prepared by reacting rapamycin with methylphosphonic dichloride and n-butanol using 3,5-lutidine in CH₂Cl₂ under a nitrogen atmosphere. Binding affinity of the rapamycin phosphorus derivs. for human FKBP-12 protein was assayed, dosages for restenosis prevention were discussed.

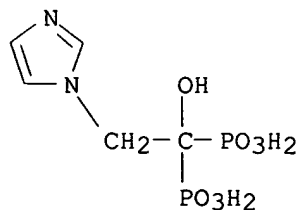
IT 118072-93-8, Zoledronate

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of phosphorus-containing rapamycin derivs. for use in pharmaceutical compns. as immunosuppressive and anticancer agents)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)

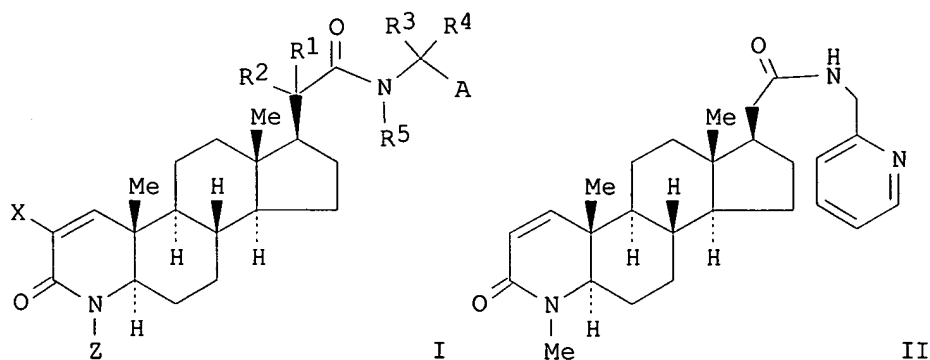


FAN.CNT 1

DATE _____

| | |
|---|---|
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| | NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, |
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| | RW: |
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| EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, | |
| SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, | |
| | SN, TD, TG |

GI



AB 3-Oxo-4-aza-5 α -androst-1-ene-17 β -acetamide derivs., such as I
[X = H, halo; Z = H, CF₃, carbonylalkyl, alkyl, alkoxy, halo, CH₂OH; A =
aromatic ring having 0-4 heteroatoms; polycyclic ring system having one or
more aromatic rings and 0-4 heteroatoms; R₁, R₂, R₃, R₄, R₅ = H, halo, alkyl,
amino, alkylamino, aminoalkyl, alkoxyalkyl, alkoxyalkyl,
alkoxycarbonylalkyl, cyano, perfluoroalkyl, alkylcarbonyl,
alkylcarbonylamino, etc.; R₁R₂, R₃R₄ = oxo, spirocycloalkyl], or a
pharmaceutically acceptable salt or an enantiomer thereof, were prepared for
their use as modulators of the androgen receptor (AR) in a tissue
selective manner. Thus, 3-oxo-4-aza-5 α -androst-1-ene-17 β -
acetamide derivative II, was prepared via a multiple step reaction sequence
starting from 4-methyl-3-oxo-4-aza-5 α -androst-1-ene-17-carboxylic
acid and 2-aminomethylpyridine. I are therefore useful in the enhancement
of weakened muscle tone and the treatment of conditions caused by androgen
deficiency or which can be ameliorated by androgen administration,

including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-wasting, prostate cancer, benign prostatic hyperplasia (BPH), cancer cachexia, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

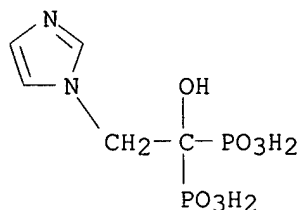
IT 118072-93-8, Zoledronate

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(bone strengthening agents as adjuvant therapeutics; preparation of 3-oxo-4-aza-5 α -androst-1-ene-17 β -acetamide derivs. as androgen receptor modulators and their therapeutic uses)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



L24 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:995989 CAPLUS

DN 142:747

TI Combination treatment with strontium for the prophylaxis and/or treatment of cartilage and/or bone conditions

IN Hansen, Christian; Nilsson, Henrik

PA Nordic Bone A/S, Den.; Osteologix A/S; Christgau, Stephan

SO PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|----------|
| PI | WO 2004098618 | A2 | 20041118 | WO 2004-DK327 | 20040506 |
| | WO 2004098618 | A3 | 20050324 | | |
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| | RW: | | | | |
| | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRAI | DK 2003-691 | A | 20030507 | | |
| | DK 2003-931 | A | 20030620 | | |
| | DK 2003-1819 | A | 20031209 | | |
| | US 2003-528548P | P | 20031209 | | |

AB A combination treatment, wherein a strontium-containing compound together with

one or more active substances capable of reducing the incidence of bone fracture and/or increasing bone d. and/or improving healing of fractured bone and/or improving bone quality are administered for use in the treatment and/or prophylaxis of cartilage and/or bone conditions.

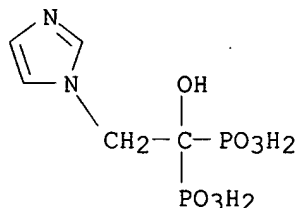
IT 118072-93-8, Zoledronate

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



L24 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:965067 CAPLUS

DN 141:406039

TI Combinations for the treatment of diseases involving cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis

IN Hilberg, Frank; Solca, Flavio; Stefanic, Martin Friedrich; Baum, Anke; Munzert, Gerd; Van Meel, Jacobus C. A.

PA Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.

SO PCT Int. Appl., 101 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| | ----- | ---- | ----- | ----- | ----- |
| PI | WO 2004096224 | A2 | 20041111 | WO 2004-EP4363 | 20040424 |
| | WO 2004096224 | A3 | 20041216 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
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| | EP 1473043 | A1 | 20041103 | EP 2003-9587 | 20030429 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| PRAI | EP 2003-9587 | A | 20030429 | | |
| | EP 2004-508 | A | 20040113 | | |
| | EP 2004-1171 | A | 20040121 | | |

AB The present invention relates to a pharmaceutical combination for the treatment of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the treatment of said diseases, comprising co-administration of effective amts. of specific active compds. and/or

co-treatment with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination preps. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

IT 118072-93-8, Zoledronic acid

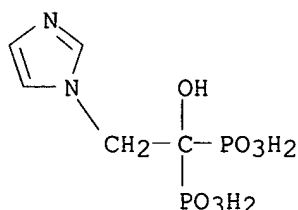
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(drug combinations for diseases involving cell proliferation and migration or apoptosis or angiogenesis including protein tyrosine kinase receptor antagonists and radiotherapy)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



L24 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:802699 CAPLUS

DN 141:294695

TI Osteoclast precursor cells as biomarkers for inflammatory joint diseases and related diagnostic and therapeutic methods

IN Ritchlin, Christopher T.; Haas-Smith, Sally; Schwarz, Edward

PA University of Rochester, USA

SO PCT Int. Appl., 214 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-----------------|--|----------|-----------------|----------|
| PI | WO 2004082635 | A2 | 20040930 | WO 2004-US8168 | 20040315 |
| | WO 2004082635 | A3 | 20050811 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | US 2004209316 | A1 | 20041021 | US 2004-799345 | 20040312 |
| PRAI | US 2003-454573P | P | 20030314 | | |
| | US 2004-799345 | A | 20040312 | | |

AB The invention discloses that the increase in osteoclast cells is preceded by an increase of osteoclast precursor cells in the peripheral blood of a subject with an inflammatory joint disease. The invention thereby discloses methods of diagnosing inflammatory joint disease and therapeutic methods for inflammatory joint disease among methods and compns. related to osteoclasts and osteoclast precursor cells. Specifically, the invention claims use of cell surface markers CD14, CD11a, CD11b,

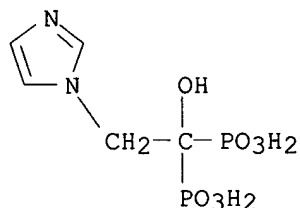
CD51/CD61, RANK, CCR1, CCR4, VCAM (CD106), VLA-4 (CD49d), CD16, MHC class II antigens, B7.1, B7.2, CD40 and c-fms to measure how many osteoclast precursor cells are in human tissue samples. Methods of diagnosing inflammatory joint diseases include measuring the number of osteoclast precursor cells, measuring osteoclast formation in culture, measuring the amount of tumor necrosis factor(TNF)- α secreted from cultured peripheral blood mononuclear cells (PBMC), measuring eroded bone material in cortical bone wafers after culturing with PBMC, and measuring mRNAs of osteoclast precursor cell markers. Similarly, the invention claims the osteoblast precursor cells and their markers in methods for monitoring therapies with anti-inflammatory agents. FACS characterization and an osteoclastogenesis assay of human TNF-transgenic mice showed that high levels of CD11b can be used as a representative marker for osteoclast precursors in the spleen. Injection of TNF α into wild-type mice induced a change in tissue distribution of CD11bhi cells similar to that observed in blood and spleen of the TNF-transgenic mice. These results suggested that redistribution of CD11bhi osteoclast precursors from bone marrow to circulation could be a mechanism for TNF α -induced erosive **arthritis**. In one example, PMBC from psoriatic **arthritis** patients were cultured to determine the osteoclast precursor cell frequency before and after anti-TNF- α therapy with Enbrel (etanercept) and infliximab. As determined by FACS of CD14/CD11b staining, the frequency of osteoclast precursors was significantly reduced in PMBC after anti-TNF therapy. Figures show a systemic lupus erythematosus-tumor necrosis factor transcriptome in blood leukocytes from children.

IT 118072-93-8

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteoclast precursor cells and cell surface-associated proteins as biomarkers for inflammatory joint diseases and related diagnostic and therapeutic methods)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



L24 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:642446 CAPLUS

DN 142:148138

TI Targeting osteoclasts with zoledronic acid prevents bone destruction in collagen-induced **arthritis**

AU Sims, Natalie A.; Green, Jonathan R.; Glatt, Markus; Schlicht, Stephen; Martin, T. John; Gillespie, Matthew T.; Romas, Evan

CS St. Vincent's Hospital, University of Melbourne, Melbourne, Australia

SO Arthritis & Rheumatism (2004), 50(7), 2338-2346

CODEN: ARHEAW; ISSN: 0004-3591

PB John Wiley & Sons, Inc.

DT Journal

LA English

AB Objective: To study the effect of zoledronic acid (ZA) on synovial inflammation, structural joint damage, and bone metabolism in rats during the effector phase of collagen-induced **arthritis** (CIA). Methods: CIA was induced in female dark agouti rats. At the clin. onset of CIA, rats were assigned to treatment with vehicle or single s.c. doses of ZA (1.0, 10, 50, or 100 μ g/kg). Clin. signs in all 4 paws were scored on

a daily basis. After 2 wk, the joints in the hind paws were assessed using plain radiographs, microfocal computed tomog. (micro-CT), histol. scoring, and histomorphometry, and the serum levels of type I collagen crosslinks were measured by ELISA. Results: Although ZA mildly exacerbated synovitis, it effectively suppressed structural joint damage. At doses of ≥ 10 $\mu\text{g/kg}$, ZA significantly reduced radiog. bone erosions, Larsen scores, and juxtaarticular trabecular bone loss as quantified by micro-CT. ZA prevented increased type I collagen (bone) breakdown in CIA and diminished histol. scores of focal bone erosion by up to 80%. Increases in the percentage of eroded surface, osteoclast surface, and osteoclast nos. associated with CIA were prevented by ZA, even though synovitis scores were unchanged. Conclusion: Single doses (≥ 10 $\mu\text{g/kg}$) of ZA strikingly reduced focal bone erosions and juxtaarticular trabecular bone loss, although synovitis was mildly exacerbated. Targeting osteoclasts with ZA may therefore be an effective strategy for preventing structural joint damage in **rheumatoid arthritis**.

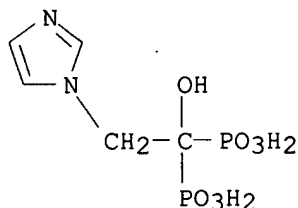
IT 118072-93-8, Zoledronic acid

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(single dose of zoledronic acid effectively reduced focal bone erosions and juxtaarticular trabecular bone loss, protected against structural joint damage, although synovitis was mildly exacerbated during effector phase in CIA rat model)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:642445 CAPLUS

DN 142:148137

TI Zoledronic acid protects against local and systemic bone loss in tumor necrosis factor-mediated **arthritis**

AU Herrak, Petra; Goertz, Birgit; Hayer, Silvia; Redlich, Kurt; Reiter, Erika; Gasser, Juerg; Bergmeister, Helga; Kollias, Giorgos; Smolen, Josef S.; Schett, Georg

CS University of Vienna, Vienna, Austria

SO Arthritis & Rheumatism (2004), 50(7), 2327-2337

CODEN: ARHEAW; ISSN: 0004-3591

PB John Wiley & Sons, Inc.

DT Journal

LA English

AB Objective: Increased osteoclast activity is a key factor in bone loss in **rheumatoid arthritis** (RA). This suggests that osteoclast-targeted therapies could effectively prevent skeletal damage in patients with RA. Zoledronic acid (ZA) is one of the most potent agents for blocking osteoclast function. We therefore investigated whether ZA can inhibit the bone loss associated with chronic inflammatory conditions. Methods: Human tumor necrosis factor (TNF)-transgenic (hTNFtg) mice, which develop severe destructive **arthritis** as well as osteoporosis, were treated with phosphate buffered saline, single or repeated doses of

ZA, calcitonin, or anti-TNF, at the onset of **arthritis**.

Results: Synovial inflammation was not affected by ZA. In contrast, bone erosion was retarded by a single dose of ZA (~60%) and was almost completely blocked by repeated administration of ZA (~95%). Cartilage damage was partly inhibited, and synovial osteoclast counts were significantly reduced with ZA treatment. Systemic bone mass dramatically increased in hTNFtg mice after administration of ZA, which was attributable to an increase in trabecular number and connectivity. In

addition,

bone resorption parameters were significantly lowered after administration of ZA. Calcitonin had no effect on synovial inflammation, bone erosion, cartilage damage, or systemic bone mass. Anti-TNF entirely blocked synovial inflammation, bone erosion, synovial osteoclast formation, and cartilage damage but had only minor effects on systemic bone mass.

Conclusion: ZA appears to be an effective tool for protecting bone from arthritic damage. In addition to their role in antiinflammatory drug therapy, modern bisphosphonates are promising candidates for maintaining joint integrity and reversing systemic bone loss in patients with **arthritis**.

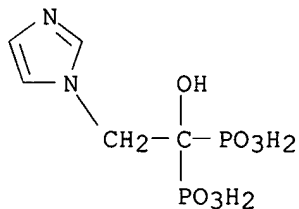
IT 118072-93-8, Zoledronic acid

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ZA did not affect synovial inflammation, retarded bone erosion, partly inhibited cartilage damage, reduced synovial osteoclast count, bone resorption parameters, increased systemic bone mass in human TNFtg mouse with **arthritis**)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:412812 CAPLUS

DN 140:406808

TI Preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators

IN Kim, Yuntae; Spencer, Keith L.; Hanney, Barbara; Duggan, Mark E.

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 136 pp.

CODEN: PIXXD2

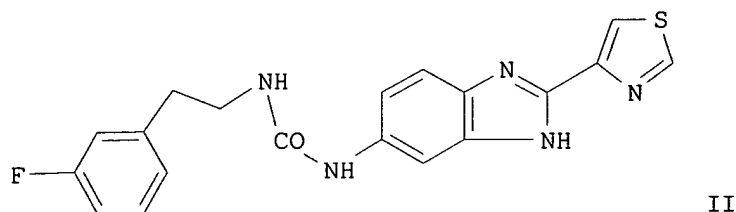
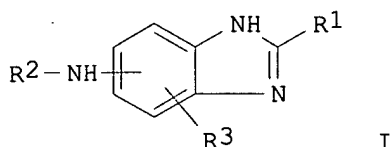
DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|----------|
| PI | WO 2004041277 | A1 | 20040521 | WO 2003-US34345 | 20031028 |
| | W: | | | | |
| | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 CA 2504044 AA 20040521 CA 2003-2504044 20031028
 EP 1581217 A1 20051005 EP 2003-777969 20031028
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 PRAI US 2002-422914P P 20021101
 WO 2003-US34345 W 20031028
 OS MARPAT 140:406808
 GI



AB Carbonylamino-benzimidazoles (shown as I; variables defined below; e.g. II) are modulators of the androgen receptor (AR) in a tissue selective manner. They are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. These compds. are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, arthritic condition and joint repair, HIV-wasting, prostate cancer, cancer cachexia, Alzheimer's disease, muscular dystrophies, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents. Although the methods of preparation are not claimed, 6 example preps. and characterization data for .apprx.150 examples of I are included; nearly all examples contain the thiazol-4-yl group at the 2 position of the benzimidazole. For example, II was prepared from 3-fluorophenethylamine, 1,1'-carbonyldiimidazole and [2-(thiazol-4-yl)-3H-benzimidazol-5-yl]amine, the latter of which was prepared from thiazole-4-carboxylic acid and (4-amino-3-nitrophenyl)carbamic acid tert-Bu ester (preparation described) via amide formation followed by cyclization in 20% aqueous AcOH. For I: R1 = aryl or heterocyclyl; R2 = -(C:O)NR5R6, -(C:O)a(C1-10)alkyl, -(C:O)a(C2-8)alkenyl, -(C:O)a(C2-8)alkynyl, -(C:O)a(C3-10)cycloalkyl, -(C:O)a(C3-8)heterocyclyl, and -(C:O)aaryl; R3 = H, halogen, -(C:O)aOb(C1-10)alkyl, -(C:O)aOb(C2-8)alkenyl, -(C:O)aOb(C2-8)alkynyl, -(C:O)aOb(C3-10)cycloalkyl, -(C:O)aOb(C3-8)heterocyclyl, -(C:O)aObaryl, -(C:O)aNR5R6, -Ob(C:O)NR5R6, -NR5(C:O)aObRb, -NR5(C:O)NR5R6, -NR5S(O)2Rb, -(C:O)OH, trifluoromethoxy, trifluoroethoxy, -Ob(C1-10)perfluoroalkyl, -S(O)2Ob(C1-10)alkyl, -S(O)2Ob(C2-8)alkenyl, -S(O)2Ob(C2-8)alkynyl,

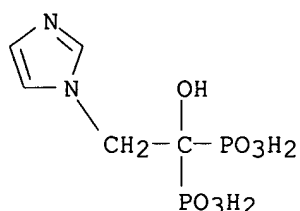
-S(O)2Ob(C3-10)cycloalkyl, -S(O)2Ob(C3-8)heterocyclyl, -S(O)2Obaryl, -NR5S(O)2NR5R6, -CN, -NO2, oxo, and -OH; a = 0-1; b = 0-1; addnl. details are given in the claims.

IT 118072-93-8, Zoledronate

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



L24 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:354800 CAPLUS

DN 140:350571

TI Method of administering bisphosphonates for the treatment of
rheumatoid arthritis

IN Sloan, Victor

PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.

SO PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2004035061 | A1 | 20040429 | WO 2003-EP11380 | 20031014 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW | | | | |
| | RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR | | | | |
| | CA 2501381 | AA | 20040429 | CA 2003-2501381 | 20031014 |
| | EP 1553958 | A1 | 20050720 | EP 2003-772213 | 20031014 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | BR 2003015328 | A | 20050816 | BR 2003-15328 | 20031014 |
| PRAI | US 2002-41855P | P | 20021015 | | |
| | WO 2003-EP11380 | W | 20031014 | | |

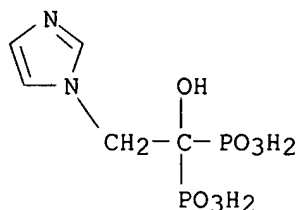
OS MARPAT 140:350571

AB Bisphosphonates, in particular more potent N-bisphosphonates such as zoledronic acid and derivs., can be used with satisfactory results for treatment of **rheumatoid arthritis** by intermittent administration, wherein the periods between bisphosphonate administrations are from about 2 mo up to about 4 mo, e.g. once every 3 mo.

IT 118072-93-8

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bisphosphonate administration for treatment of **rheumatoid arthritis**)

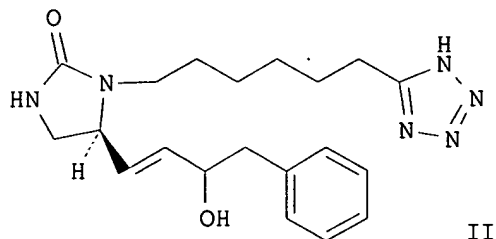
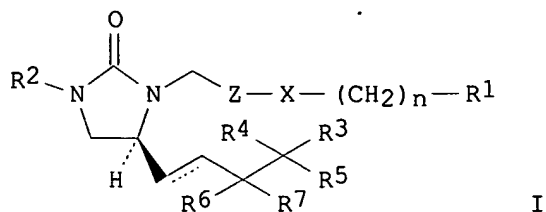
RN 118072-93-8 CAPLUS
 CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA
 INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2003:991344 CAPLUS
 DN 140:42461
 TI Preparation of asparagine-derived 1,5-disubstituted imidazolidin-2-one
 derivatives for use as EP4 receptor agonists in the treatment of eye and
 bone diseases
 IN Billot, Xavier; Young, Robert N.
 PA Merck Frosst Canada & Co., Can.
 SO PCT Int. Appl., 60 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2003103664 | A1 | 20031218 | WO 2003-CA842 | 20030603 |
| | W: | | | | |
| | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, | | | | |
| | CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, | | | | |
| | GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, | | | | |
| | LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, | | | | |
| | PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, | | | | |
| | UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: | | | | |
| | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, | | | | |
| | KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, | | | | |
| | FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, | | | | |
| | BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2487977 | AA | 20031218 | CA 2003-2487977 | 20030603 |
| | EP 1513523 | A1 | 20050316 | EP 2003-727101 | 20030603 |
| | R: | | | | |
| | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | | |
| | IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| PRAI | US 2002-386641P | P | 20020606 | | |
| | WO 2003-CA842 | W | 20030603 | | |
| OS | MARPAT 140:42461 | | | | |
| GI | | | | | |



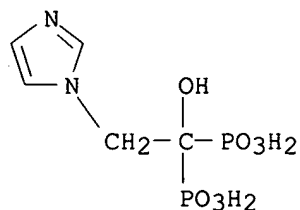
AB The invention relates to imidazolidinones I [X is a bond, O or S; R1 is OH, CN, carboxyalkyl, CF2SO2NH2, SO2NH2, PO3H2, heterocyclyl, etc.; R2 is H, aryl, or alkyl; R3, R4 are H, halo, or alkyl; R5 is (hetero)aryl or (hetero)cycloalkyl or alkyl substituted by these groups; CR6R7 is CO or CH(OH); Z is (CRb2)0-4 or CRb:CRb, where Rb is H, halo, alkyl, or cycloalkyl; n is 0-4] or their pharmaceutically-acceptable salts, enantiomers, diastereomers, prodrugs or mixts., which are potent selective agonists of the EP4 subtype of prostaglandin E2 receptors, and their use in the treatment of glaucoma and other conditions which are related to elevated intraocular pressure in the eye and for mediating the bone modeling and remodeling processes of the osteoblasts and osteoclasts. Thus, R-asparagine-derived benzyl (4R)-3-(6-cyanoethyl)-4-formyl-2-oxoimidazolidine-1-carboxylate was treated with PhCH2COCH2P(O)(OMe)2, NaBH4, and Bu3SnN3 to afford tetrazole derivative II.

IT 118072-93-8

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical ingredient; preparation of asparagine-derived imidazolidinone derivs. for use as EP4 receptor agonists in treatment of eye and bone diseases)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:757525 CAPLUS

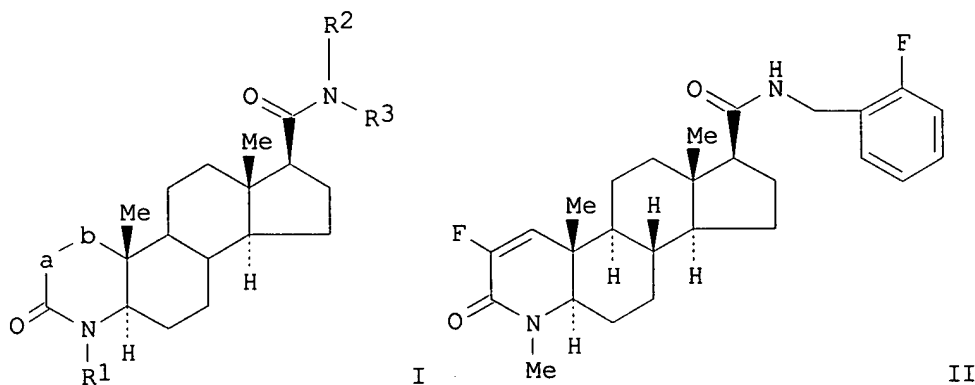
DN 139:277056

TI Preparation of fluorinated 4-aza-androstan-3-one-17β-carboxamide derivatives as androgen receptor modulators

IN Meissner, Robert S.; Perkins, James J.

PA Merck & Co., Inc., USA
 SO PCT Int. Appl., 95 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2003077919 | A1 | 20030925 | WO 2003-US8277 | 20030307 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2478186 | AA | 20030925 | CA 2003-2478186 | 20030307 |
| | EP 1485095 | A1 | 20041215 | EP 2003-714228 | 20030307 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, SK | | | | |
| | BR 2003008355 | A | 20050125 | BR 2003-8355 | 20030307 |
| | US 2005165039 | A1 | 20050728 | US 2003-507239 | 20030307 |
| | JP 2005526082 | T2 | 20050902 | JP 2003-575972 | 20030307 |
| PRAI | US 2002-363822P | P | 20020313 | | |
| | WO 2003-US8277 | W | 20030307 | | |
| OS | MARPAT 139:277056 | | | | |
| GI | | | | | |



AB Fluorinated 4-aza-androstan-3-one-17 β -carboxamide derivs., such as I [a-b = CF:CH, CHFCH₂, CF₂CH₂; R₁ = H, CH₂OH, (un)substituted alkyl; R₂ = H, alkyl; R₃ = alkyl, cycloheteroalkyl, aryl, heteroaryl; R₂R₃ = 5 or 6-membered ring fused with a 5- or 6-membered aromatic ring system having 0-2 heteroatoms], or a pharmaceutically acceptable salt or an enantiomer thereof, were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 4-aza-androstan-3-one-17 β -carboxamide derivative II, was prepared via a multiple step reaction sequence starting from 4-methyl-4-aza-androstan-3-one-17-carboxylic acid Me ester and 2-fluoro-benzylamine. The prepared compds. are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. I are therefore useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration,

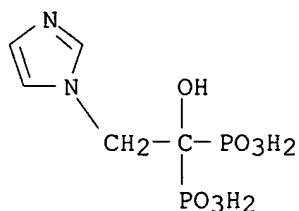
including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-wasting, prostate cancer, cancer cachexia, muscular dystrophies, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

IT 118072-93-8, Zoledronate

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone strengthening agents as adjuvant therapeutics; preparation of fluorinated 4-aza-androstan-3-one-17 β -carboxamide derivs. as androgen receptor modulators and their therapeutic uses)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:652131 CAPLUS

DN 139:214237

TI Preparation of nitrate prodrugs able to release nitric oxide in a controlled and selective way and their use for prevention and treatment of inflammatory, ischemic and proliferative diseases

IN Scaramuzzino, Giovanni

PA Italy

SO Eur. Pat. Appl., 313 pp.

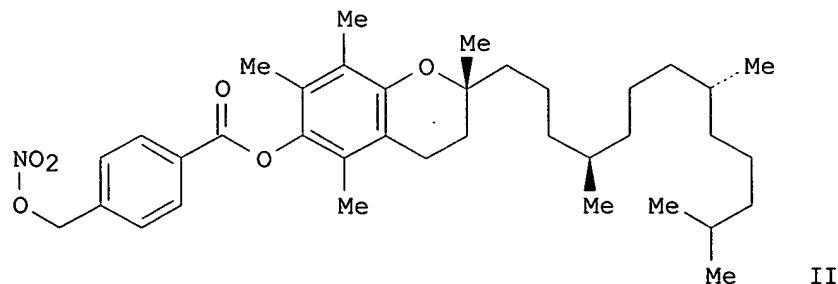
CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | EP 1336602 | A1 | 20030820 | EP 2002-425075 | 20020213 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| PRAI | EP 2002-425075 | | 20020213 | | |
| GI | | | | | |



II

AB New pharmaceutical compds. of general formula F-(X)_q (I) [q = 1-5, preferably 1; F is chosen among drugs such as δ-tocopherol, clidanac, diethylhomospermine, glucosamine, thymocartin, vofopitant, etc.; X is chosen among 4 groups M, T, V, and Y where M = ONO₂, nitrate salt, nitrite ester, ONO, thionitrite, SNO, etc., T = OR₁-M, OR₁OR₁-M, SR₁NR₂R₁-M, NR₂R₁-M, NR₂R₁SR₁-M, etc., R₁ = saturated or unsatd., linear or branched alkylene, having 1 to 21 carbon atoms or a saturated or unsatd., optionally heterosubstituted or branched cycloalkylene, having 3 to 7 carbon atoms or an optionally heterosubstituted arylene having 3 to 7 carbon atoms; R₂ = H, saturated or unsatd., linear or branched 1-21 carbon atom alkyl, saturated or unsatd. optionally heterosubstituted or branched 3-7 carbon cycloalkyl, optionally heterosubstituted 3-7 carbon aryl; R₁, R₂ = OH, SH, F, Cl, Br, OPO₃H₂, CO₂H, etc.; bond between F and T = carboxylic ester, carboxylic amide, glycoside, azo, thioester, sulfonic ester, etc.; V = Z-M₂, OZ-M₂, NR₂Z-M₂, R₁Z-M₂, OR₁-M₂, OR₁Z-M₂, M₂ = M, R₁-M, OR₁-M, SR₁-M, NR₂R₁-M; ZM₂ = COCH₂CH(M₂)CH₂N+Me₃, COCH₂CH₂COM₂, COCH(NHR₂)CH₂M₂, etc.; Y = 4-COC₆H₄CH₂ONO₂, O(CH₂)₄ONO₂, COCH(NH₂)CH₂ONO₂, 3-OC₆H₄CH₂ONO₂, etc.] were prepared For example, α-tocopherol reacted with 4-HO₂CC₆H₄CH₂ONO₂ to give the nitroxymethyl derivative II. The compds. of general formula I are nitrate prodrugs which can release nitric oxide in vivo in a controlled and selective way and without hypotensive side effects and for this reason they are useful for the preparation of medicines for prevention and treatment of inflammatory, ischemic, degenerative and proliferative diseases of musculoskeletal, tegumental, respiratory, gastrointestinal, genito-urinary and central nervous systems.

IT 586348-36-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

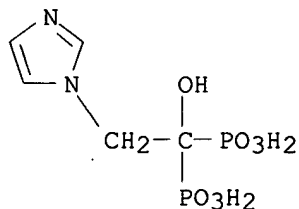
RN 586348-36-9 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis-, mononitrate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 118072-93-8

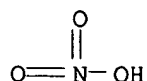
CMF C5 H10 N2 O7 P2



CM 2

CRN 7697-37-2

CMF H N O3



RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:454048 CAPLUS
DN 139:30847
TI EP4 receptor agonists, preparation thereof, pharmaceutical compositions,
and therapeutic uses
IN Ogidigben, Miller J.; Young, Robert N.; Billot, Xavier; Metters, Kathleen
M.; Slipetz, Deborah M.
PA Merck & Co., Inc., USA; Merck Frosst Canada & Co.
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2003047417 | A2 | 20030612 | WO 2002-US38039 | 20021127 |
| | WO 2003047417 | A3 | 20031127 | | |
| | W: | | | | |
| | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, | | | | |
| | CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, | | | | |
| | GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, | | | | |
| | LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, | | | | |
| | PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, | | | | |
| | UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: | | | | |
| | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, | | | | |
| | KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, | | | | |
| | FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, | | | | |
| | CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2466751 | AA | 20030612 | CA 2002-2466751 | 20021127 |
| | EP 1453503 | A2 | 20040908 | EP 2002-784629 | 20021127 |
| | R: | | | | |
| | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | | |
| | IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| | JP 2005519879 | T2 | 20050707 | JP 2003-548683 | 20021127 |
| | US 2004204590 | A1 | 20041014 | US 2004-493649 | 20040422 |
| PRAI | US 2001-337228P | P | 20011203 | | |
| | WO 2002-US38039 | W | 20021127 | | |

OS MARPAT 139:30847

AB The invention discloses potent selective agonists of the EP4 subtype of
prostaglandin E2 receptors, formulations thereof, preparation thereof, and use
thereof in the treatment of glaucoma and other conditions which are
related to elevated intraocular pressure in the eye of a patient. The
invention further discloses the use of these compds. for mediating the
bone modeling and remodeling processes of the osteoblasts and osteoclasts.

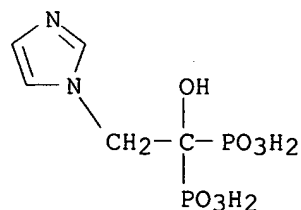
IT 118072-93-8, Zoledronate

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(EP4 receptor agonists, preparation, pharmaceutical compns., therapeutic
uses, and use with other agents)

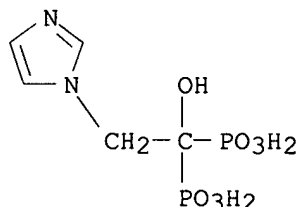
RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA
INDEX NAME)



L24 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2002:794290 CAPLUS
 DN 137:284400
 TI Bisphosphonate compounds for inhibiting farnesyl diphosphate synthase
 IN Bergstrom, James D.; Reszka, Alfred A.; Rodan, Gideon A.
 PA Merck & Co., Inc., USA
 SO U.S. Pat. Appl. Publ., 11 pp., Cont. of U. S. Ser. No. 513,150.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 1

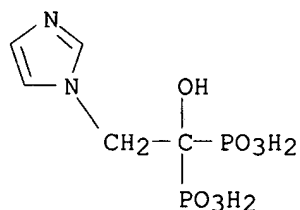
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | US 2002151459 | A1 | 20021017 | US 2002-121465 | 20020411 |
| | US 2004235797 | A1 | 20041125 | US 2004-877094 | 20040625 |
| PRAI | US 2000-513150 | A1 | 20000225 | | |
| | US 2002-121465 | A1 | 20020411 | | |
| OS | MARPAT 137:284400 | | | | |
| AB | The present invention relates to methods for identifying compds. useful as inhibitors of farnesyl diphosphate synthase. More particularly, the compds. so identified are useful for inhibiting bone resorption. The present invention also relates to methods for inhibiting bone resorption in a mammal comprising administering to a mammal in need thereof a therapeutically effective amount of a farnesyl diphosphate synthase inhibitor. Thus, tablets contained farnesyl diphosphate synthase inhibitor 0.10-10, anhydrous lactose 71.32, Mg stearate 1.0, Croscarmellose sodium 2.0, and microcryst. cellulose qs 200 mg. | | | | |
| IT | 118072-93-8 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (bisphosphonate compds. for inhibiting farnesyl diphosphate synthase) | | | | |
| RN | 118072-93-8 CAPLUS | | | | |
| CN | Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME) | | | | |



L24 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2002:428720 CAPLUS
 DN 137:746
 TI Use of bisphosphonates for pain treatment
 IN Fox, Alyson; Green, Jonathan; O'Reilly, Terence; Urban, Laszlo; Walker, Katharine
 PA Novartis Ag, Switz.; Novartis-Erfindungen Verwaltungsgesellschaft M.B.H.
 SO PCT Int. Appl., 22 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| PI | WO 2002043738 | A2 | 20020606 | WO 2001-EP13836 | 20011127 |
| | WO 2002043738 | A3 | 20030327 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, | | | | |

HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU,
 LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG,
 SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, ZW
 RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR
 CA 2427161 AA 20020606 CA 2001-2427161 20011127
 AU 2002017061 A5 20020611 AU 2002-17061 20011127
 EP 1339411 A2 20030903 EP 2001-998352 20011127
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 BR 2001015696 A 20040210 BR 2001-15696 20011127
 JP 2004514696 T2 20040520 JP 2002-545708 20011127
 CN 1535152 A 20041006 CN 2001-819784 20011127
 NZ 525871 A 20050429 NZ 2001-525871 20011127
 ZA 2003003247 A 20040510 ZA 2003-3247 20030425
 NO 2003002405 A 20030527 NO 2003-2405 20030527
 US 2004063670 A1 20040401 US 2003-432847 20031002
 PRAI GB 2000-29111 A 20001129
 WO 2001-EP13836 W 20011127
 OS MARPAT 137:746
 AB A method for the treatment of pain, in particular antinociceptive or
 anti-allodynic treatment of pain, in a patient in need of such treatment,
 e.g. a patient with osteoporosis or osteopenia, a tumor patient, or a
 patient suffering from an inflammatory disease, comprises administering an
 effective amount of a bisphosphonate, e.g. zoledronic acid or salts or
 hydrates thereof, to the patient.
 IT 118072-93-8, Zoledronic acid
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (bisphosphonates for pain treatment)
 RN 118072-93-8 CAPLUS
 CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA
 INDEX NAME)



L24 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2000:891342 CAPLUS
 DN 135:55654
 TI Changes in cross-sectional geometry of the distal femoral metaphysis
 associated with inflammatory **arthritis** are reduced by a
 bisphosphonate (zoledronate)
 AU Pysklywec, Michael W.; Moran, Erica L.; Bogoch, Earl R.
 CS Orthopaedic Research Laboratory, University of Toronto, Toronto, ON, M4Y
 1J3, Can.
 SO Journal of Orthopaedic Research (2000), 18(5), 734-738
 CODEN: JOREDR; ISSN: 0736-0266
 PB Journal of Bone and Joint Surgery, Inc.
 DT Journal
 LA English
 AB An increased risk of fracture is a feature of **rheumatoid
 arthritis** and of animal models of inflammatory **arthritis**
 . The authors examined geometrical changes in the metaphyseal cortex of the
 distal femur in an animal model of inflammatory **arthritis**.
 Addnl., the authors examined the effect of a bisphosphonate in preventing

these changes. 5 Groups of rabbits were studied: normal controls, those with inflammatory **arthritis**, and 3 groups with **arthritis** treated with bisphosphonate. To determine geometrical properties, image anal. was performed on digitized cross sections of the femoral metaphyseal cortices. The results demonstrated that the posterior cortical wall was less thick in rabbits with **arthritis** than in normal rabbits and in the rabbits in the 3 bisphosphonate treatment groups. Moment of inertia about the lateral-medial axis was reduced in rabbits with **arthritis** compared with normal rabbits. Cross-sectional area was not different between groups. The changes suggest a mechanism of weakening of bone in **arthritis**; when the results are coupled with results of previous porosity studies, severe directional weakness is apparent. Bisphosphonate was effective in preserving bone integrity in inflammatory **arthritis**.

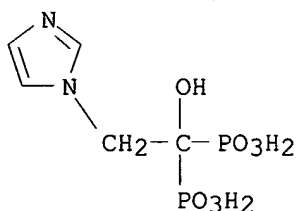
IT 118072-93-8, Zoledronate

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(zoledronate reduces **arthritis**-induced geometrical changes in distal femoral metaphysis)

RN 118072-93-8 CAPLUS

CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:666718 CAPLUS

DN 133:252041

TI Preparation of amine derivatives as cathepsin K and cathepsin S inhibitors and in treating pathology and/or symptomatology of diseases caused by cysteine protease activity

IN Link, John O.; Martelli, Arnold J.; Martichonok, Valeri; Patterson, John W.; Saunders, Oliver L.; Zipfel, Sheila

PA Axys Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 223 pp.

CODEN: PIXXD2

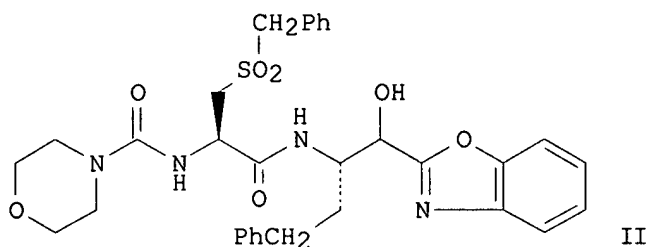
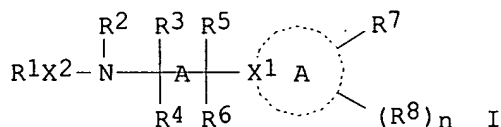
DT Patent

LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2000055144 | A1 | 20000921 | WO 2000-US6885 | 20000315 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2367352 | AA | 20000921 | CA 2000-2367352 | 20000315 |

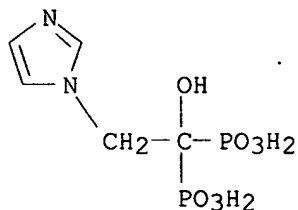
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|---|----|----------|-------------------|----------|
| EP 1161422 | A1 | 20011212 | EP 2000-916397 | 20000315 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| BR 2000009044 | A | 20020115 | BR 2000-9044 | 20000315 |
| TR 200103335 | T2 | 20020422 | TR 2001-200103335 | 20000315 |
| JP 2002539201 | T2 | 20021119 | JP 2000-605574 | 20000315 |
| EE 200100486 | A | 20030217 | EE 2001-486 | 20000315 |
| US 6576630 | B1 | 20030610 | US 2000-525507 | 20000315 |
| AU 774664 | B2 | 20040701 | AU 2000-37507 | 20000315 |
| AU 2000037507 | A5 | 20001004 | | |
| EP 1516877 | A1 | 20050323 | EP 2004-15656 | 20000315 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| ZA 2001007496 | A | 20021211 | ZA 2001-7496 | 20010911 |
| NO 2001004483 | A | 20011101 | NO 2001-4483 | 20010914 |
| BG 105969 | A | 20020531 | BG 2001-105969 | 20011002 |
| HR 2001000736 | A1 | 20021231 | HR 2001-736 | 20011012 |
| US 2003232864 | A1 | 20031218 | US 2003-354888 | 20030128 |
| PRAI US 1999-124421P | P | 19990315 | | |
| EP 2000-916397 | A3 | 20000315 | | |
| US 2000-525507 | A1 | 20000315 | | |
| WO 2000-US6885 | W | 20000315 | | |
| OS MARPAT 133:252041 | | | | |
| GI | | | | |



AB Title compds. [I; A = heteromonocyclic ring containing 5-6 member; fused heteropolycyclic ring containing 8-14 member; X¹ = C, CH; X² = bond, NHCH₂CO, NHCH₂CH₂SO₂, alkylamino; R¹ = alkylaminocarbonyl, alkoxycarbonyl, alkylcarbonyl, alkylsulfonyl; R² = H, alkyl; R³ = alkyl; R⁴ = H, alkyl; R³R⁴ = cycloalkylene, heterocycloalkylene; R⁵ = H; R⁶ = H; R⁵R⁶ = oxo; R⁷ = CN, Cl, Br, F, NO₂, H; R⁸ = alkyl, alkylidene, CN, Cl, F, Br, NO₂; n = 0, 1, 2, 3], N-oxide derivs., prodrug derivs., protected derivs., individual isomers, mixts. of isomers, and pharmaceutically acceptable salts and compns. with bisphosphonic acids or acid esters as excipients are prepared as cathepsin K and cathepsin S inhibitors. Title compds. are administering to animal in treating diseases which cysteine protease activity contributes to the pathol. and/or symptomatol. The diseases are autoimmune disorder, allergic disorder, allogeneic immune response, excessive elastolysis, cardiovascular disorders, fibril formation, etc. Thus, the title compound II was prepared

IT 118072-93-8
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (preparation of amine derivs. as cathepsin K and cathepsin S inhibitors)

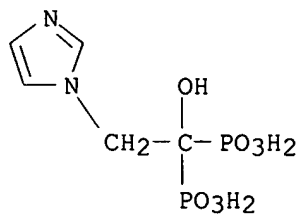
useful in disorders caused by cysteine protease activity)
 RN 118072-93-8 CAPLUS
 CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2000:456892 CAPLUS
 DN 133:68937
 TI Interleukin-6 production inhibitors
 IN Koike, Junzo; Funaba, Yuriko; Tanahashi, Masahiko; Okazaki, Seiji; Ito, Masatoshi
 PA Toray Industries, Inc., Japan
 SO PCT Int. Appl., 32 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2000038693 | A1 | 20000706 | WO 1999-JP3346 | 19990623 |
| | W: CA, CN, JP, US | | | | |
| | RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | CA 2321864 | AA | 20000706 | CA 1999-2321864 | 19990623 |
| | EP 1057488 | A1 | 20001206 | EP 1999-926772 | 19990623 |
| | R: DE, ES, FR, GB, IT | | | | |
| | US 6579860 | B1 | 20030617 | US 2000-623014 | 20000927 |
| PRAI | JP 1998-370150 | A | 19981225 | | |
| | WO 1999-JP3346 | W | 19990623 | | |
| OS | MARPAT 133:68937 | | | | |
| AB | The invention relates to drugs effective in the prevention and treatment of diseases due to abnormal production of interleukin-6, which are interleukin-6 production inhibitors containing as the active ingredient methanebis-phosphonic acid derivs. and exhibit an inhibitory effect against the production of interleukin-6. These drugs can be expected to be effective in the prevention and treatment of diseases in which interleukin-6 participates, for example, thrombocytosis, inflammatory diseases, immune response disorders, osteoporosis, rheumatoid arthritis , hypercalcemia, multiple myeloma, cachexia and nephritis. | | | | |
| IT | 118072-93-8 | | | | |
| | RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) | | | | |
| | (interleukin-6 production inhibitors for therapeutic use) | | | | |
| RN | 118072-93-8 CAPLUS | | | | |
| CN | Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis- (9CI) (CA INDEX NAME) | | | | |



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

| | | |
|--|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 117.86 | 960.71 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | -16.06 | -16.06 |

STN INTERNATIONAL LOGOFF AT 17:33:41 ON 25 OCT 2005